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globally should start to enable clinicians to better formulate accurate future diagnoses and at times prognoses.

S06. Methylation quantitation trait loci and transcriptome analysis of differentially methylated microRNAs in end-stage renal disease

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MicroRNAs are understood to play a functional role within the establishment of epigenetic marks and are in turn under epigenetic control. Emerging evidence suggests microRNAs are vital for both kidney development and renal function. This study aimed to identify differential methylation affecting microRNAs in patients with end-stage renal disease (ESRD).

Methylation status was determined for 485,577 unique CpG sites in 105 individuals with ESRD and 52 donor controls with no evidence of renal disease using the HumanMethylation450K BeadChip array (Illumina). Statistically significant associations ($P < 10^{-8}$) were observed between case and control groups for both unique CpG sites within microRNAs and their target genes, identified using miRDB (an online database for microRNA target prediction and functional annotations).

CpG sites ($n=11$) within top-ranked microRNAs ($n=42$) alongside 848 CpGs in 198 target genes were evaluated in genotyped renal transplant samples to detect methylation quantitative trait loci (meQTLs) associated with ESRD. Following allelic association PLINK analysis, 116 SNPs were determined from the investigated CpG sites, 12 of which were located in genes previously linked with renal disease or microRNAs.

Blood-derived Ion Total RNA-Seq v2 analysis was performed on 10 ESRD samples and 29 controls (with no evidence of renal disease) to determine the expression levels of the microRNAs and target genes. Sequencing was completed using the Ion Proton™ (Thermo Fisher Scientific) and the most significant results were *MIR548H4* (5.79×10^{-6}) and *WASF3* (5.59×10^{-9}) respectively, showing increased expression within the ESRD samples.

This study has identified microRNA-related differential methylation with supporting gene expression data, associated with ESRD.

S07. Genetic overlap between amyotrophic lateral sclerosis and schizophrenia

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Amyotrophic lateral sclerosis (ALS) is a complex neurodegenerative disease characterized by rapid-onset loss of upper and lower motor neurones, resulting in progressive paralysis and death from respiratory failure. Schizophrenia is a neuropsychiatric disease with positive symptoms, negative symptoms and impairment over a range of cognitive abilities. We have recently shown that schizophrenia occurs more frequently than expected in the pedigrees of ALS patients, suggesting an aetiological relationship between both diseases. Using linkage disequilibrium score regression with summary statistics for GWAS of ALS and schizophrenia comprising over 100,000 unique individuals, we estimated the genetic correlation between ALS and schizophrenia to be 14.3% (95% CI 7.05-21.6; $p = 1 \times 10^{-4}$). Up to 0.12% of the variance in ALS was explained by schizophrenia polygenic risk scores ($p = 8.4 \times 10^{-10}$). We leveraged the apparent pleiotropic relationship between ALS and schizophrenia to identify five potential novel ALS-associated genomic loci at conditional false discovery rate < 0.01 . Diagnostic misclassification in the schizophrenia cohort did not contribute significantly to our observations (BUHMBOX $p = 0.94$) and we estimated that 4.86% (2.47-7.13%) of ALS cases would need to be misdiagnosed as schizophrenia to observe our genetic correlation estimate under a true genetic correlation of 0%. Our results indicate that the lifetime risk for comorbid ALS and schizophrenia increases from 1 in 40,000 to 1 in 34,336, which would require an incident cohort of 16,488 ALS patients to observe epidemiologically. Our findings suggest shared underlying biology between ALS and schizophrenia which will direct novel approaches in research and therapeutic development.

S08. Identifying clinically relevant imprinted gDMRs sensitive to a transient loss of DNA methylation in human differentiated cells

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Background: Imprinted genes are autosomal, but only expressed from one parental allele and are often clustered in small groups. They play an important role in the regulation of normal mammalian

